UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,356	10/06/2003	Chiaki Ishii	58600-8229.US00	5651

79975 7590 11/09/2011

King & Spalding LLP
P.O. Box 889
Belmont, CA 94002-0889

EXAMINER	
POPA, ILEANA	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
11/09/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/680,356
Filing Date: October 06, 2003
Appellant(s): ISHII ET AL.

Jacqueline F. Mahoney
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 08/05/2011 appealing from the Office action mailed 01/05/2011.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 1-4, 6-12 and 22-25.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

WO98/23948	Boxer et al.	6-1998
DE 19902391	Niemeyer et al.	1-1999
5,874,316	Cornell et al.	2-1999
5,310,648	Arnold et al.	5-1994
6,051,372	Bayerl et al.	4-2000
2003/0148335	Shen et al.	10-2001

Boukobza et al., "Immobilization in surface-tethered lipid vesicles as a new tool for single molecule spectroscopy", J Phys Chem, 2001, vol. 105, pp. 12165-12170.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6, 7, 9, 11, 12 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al. (WO98/23948), in view of both Boukobza et al. (J Phys Chem, 2001, 105: 12165-12170) and Niemeyer et al. (DE 19902391).

Boxer et al. teach a surface detector array device comprising a substrate defining a plurality of distinct bilayer-compatible surface regions separated by one or more bilayer barrier regions, a bulk aqueous phase covering the substrate surface, a lipid bilayer expanse carried on each of the bilayer-compatible region, and an aqueous film interposed between each bilayer-compatible region and the corresponding lipid bilayer expanse, i.e., the aqueous film is interposed between the bilayer-compatible surface region and the lower surface of the corresponding bilayer expanse (claims 1 and 9) (p. 4, lines 5-12). Boxer et al. teach that the bilayer expanses may be modified so that they comprise lipids coupled to biomolecules such as transmembrane receptors wherein each bilayer expanse could have a specific biomolecule and wherein the biomolecules can be non-covalently attached to the bilayer via specific molecular interactions such as

biotin/avidin interactions (claims 1, 22, and 23) (Abstract; p. 4, line 32 through p. 5, line 5). Therefore, Boxer et al. teach that the lipid bilayer expanses have different compositions (claim 3). Boxer et al. teach using their device to detect a selected ligand (i.e., a test agent) in a mixture of ligands, specifically by contacting the device with the mixture of ligands and detecting the binding of the selected ligand to its receptor immobilized on the device (p. 5, lines 14-17; p. 21, lines 10-16). *Thus, the device of Boxer et al. comprises receptors associated with the lipid bilayer having the ligand binding sites located on the exterior of the lipid bilayer, wherein the exposed binding sites are capable of specifically binding test agents* (claim 1). With respect to the limitation of inner and outer surfaces (claim 1), a bilayer lipid necessarily has inner and outer surfaces; therefore, Boxer et al. do teach lipid bilayer expanses with an inner and an outer bilayer surface (compare also Fig. 1 of the international publication WO98/23948 with Fig. 1 of the instant application, both depicting the same composition). Boxer et al. teach that the bilayers could comprise lipids covalently coupled to polynucleotides (p. 16, lines 3-21). The bilayer-compatible surface regions may be formed of materials such as SiO_2, MgF_2, CaF_2, and mica (claim 11) and the bilayer expanse may comprise phosphatidylcholine (claim 12) (p. 4, lines 13-15 and 20-24). Boxer et al. also teach that one embodiment relates to sorting devices for biomolecules integrated or attached to the supported bilayer, wherein the device comprises barrier regions acting as two dimensional sieves having progressively smaller openings that are capable to sort the membrane-associated molecule by size,

i.e., the array comprises discrete bilayer patches associated with the lipid bilayer expanses (claim 2) (p. 25 bridging p. 26 and Fig. 5).

Boxer et al. do not teach vesicles or that their receptors are associated with the vesicles (claims 1 and 24), nor do they teach second biomolecules associated with the bilayer expanses wherein the second biomolecules are capable of freely moving within the expanse (claim 6) or that some of the bilayer expanses have different second molecules (claim 7). However, using such is suggested by the prior art. For example, Boukobza et al. teach that directly immobilizing test biomolecules on substrates modifies their dynamics via interaction with the substrate. Boukobza et al. teach overcoming the biomolecule-substrate interaction by using a novel immobilization technique comprising trapping a single soluble protein molecules inside 100 nm lipid vesicles (i.e., a first and a second biomolecule) and tethering the vesicles to a supported lipid bilayer via biotin-avidin interactions (claims 1, 6, and 24) (Abstract; p. 12165, column 2, second paragraph; p. 12166, Fig. 1). *Boukobza et al. teach that surface-tethered vesicles can also be used for experiments on reconstituted membrane proteins*, which experiments might require immobilization via lipid vesicles (p. 12169, column 2, *Conclusion*). Based on these teachings, one of skill in the art would have known that the direct immobilization of receptors as in Boxer et al. would lead to interaction with the substrate and thus interference with the receptor-ligand interaction dynamics; one of skill in the art would have also known that transmembrane receptors (i.e., membrane proteins) could be incorporated into lipid vesicles and that doing such would eliminate the interaction between the transmembrane receptors and the

substrate. It would have been obvious to one of skill in the art, at the time the invention was made, to modify the array of Boxer et al. by using the novel immobilization technique of Boukobza et al. (i.e., associating the transmembrane receptors with lipid vesicles and tethering the vesicles to the surface detector array device of Boxer et al.), with a reasonable expectation of success. One of skill in the art would have been motivated to do so in order to avoid the interaction between the transmembrane receptor and the substrate. One of skill in the art would have reasonably expected to be successful in doing such because the prior art teaches that membrane proteins can be successfully incorporated into lipid vesicles and that lipid vesicles can be successfully tethered to lipid bilayer such as the ones of Boxer et al. *By doing such, one of skill in the art would have obtained a device comprising vesicles associated with receptors having their binding sites located on the exterior of the vesicles, these receptors being capable of specifically binding test agents*.

Boxer et al. and Boukobza et al. teach tethering via biotin/avidin interactions and not via oligonucleotide hybridization (claim 1). However, doing such is suggested by the prior art. For example, Niemeyer et al. teach that tethering via oligonucleotide hybridization offers advantages over the other tethering means such as biotin/avidin interactions in that: **(i)** it permits the efficient and simultaneous immobilization of many different macromolecules in a single reaction step at specific places on the substrate; and **(ii)** it allows the regeneration of the substrate for multiple uses (p. 3; p. 4, first full paragraph; Example 1). Niemeyer et al. teach that the macromolecules could be vesicles (p. 8, first paragraph). It would have been obvious to one of skill in the art, at

the time the invention was made, to modify the array of supported bilayers of Boxer et al. and Boukobza et al. by tethering their vesicles via oligonucleotide hybridization, with a reasonable expectation of success. One of skill in the art would have been motivated to do such in order to obtain reusable expanses with different vesicle composition, each vesicle being encoded by a specific oligonucleotide, as needed. One of skill in the art would have been expected to have a reasonable expectation of success in doing so because Boxer et al. teaches that lipids covalently coupled to nucleic acids (i.e., oligonucleotides) can be easily incorporated into the lipid bilayers and because Niemeyer et al. teach that oligonucleotides incorporated into supports can be successfully used to tether to the supports macromolecules and vesicles functionalized with the complementary oligonucleotides.

With respect to the limitation recited in claim 6, absent evidence to the contrary, the protein-loaded vesicles are able to freely move within the expanse. With respect to the limitation recited in claim 7, one of skill in the art would have been motivated to use different second molecules in order to study the reconstitution of several membrane proteins at the same time. With respect to the limitation recited in claim 25, one of skill in the art would have known to use oligonucleotides with different lengths such as to optimize the results.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Claims 1-4, 6, 7, 9-12 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al. taken with both Boukobza et al. and Niemeyer et al., in further view of each Cornell et al. (U.S. Patent No. 5, 874,316), Arnold et al. (U.S. Patent 5, 310, 648), and Bayerl et al. (U.S. Patent No. 6,051,372).

The teachings of Boxer et al., Boukobza et al., and Niemeyer et al. are applied as above for claims 1-4, 6, 7, 9, 11, 12 and 22-25.

Boxer et al., Boukobza et al., and Niemeyer et al. do not teach the use of self-limiting lateral diffusion to separate the lipid regions from one another (claim 10). However, at the time the invention was made, self-limiting lateral diffusion to separate the lipid regions from one another was taught by the prior art. For example, Cornell et al. teach receptor membranes, wherein the monomers in the membrane may be prevented from diffusing laterally by selecting lipids that are crystalline at room temperature, which eliminates lateral diffusion (column 3, lines 25-29). Arnold et al. teach an imprinted matrix, wherein the spatial organization of molecules in the substrate can be locked into place by a variety of means to form a structure incapable of lateral diffusion, for example by decreasing fluidity (column 7, lines 11-24, column 8, lines 1-10). Bayerl et al. teach patterned surfaces, wherein the lateral diffusion can be prevented by switching the lipid bilayer phase to gel or crystalline and wherein the phase transition can be accomplished by adjusting one physical parameter, the temperature (column 4, lines 25-58, column 5, lines 4-25, column 7, lines 1-24, column 9, lines 32-53). It would have been obvious to one of skill in the art, at the time the indention was made, to maintain the substrate orientation by limiting the lateral diffusion

as taught by Cornell et al., Arnold et al., or Bayerl et al., with a reasonable expectation of success. One of skill in the art would have been motivated to do so because the prior art teaches that the use of self-limiting lateral diffusion to keep the lipid regions apart obviates the need for physical barriers on the substrate surface. One of skill in the art would have been expected to have a reasonable expectation of success in using any of the above-mentioned techniques because the art teaches the successful use of such techniques to limit lateral diffusion between discrete lipid regions.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Claims 1-4, 6-9, 11, 12 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al. taken with both Boukobza et al. and Niemeyer et al., in further view of Shen et al. (PGPUB 2003/0148335).

The teachings of Boxer et al., Boukobza et al., and Niemeyer et al. are applied as above for claims 1-4, 6, 7, 9, 11, 12 and 22-25.

Boxer et al., Boukobza et al., and Niemeyer et al. do not teach the identity of the biomolecule being determined from the sequence of the oligonucleotide (claim 8). Shen et al. teach the use of oligonucleotide identification tags for assaying the identity of non-nucleic acid targets, wherein the method can be used to identify any non-nucleic acid target associated with any surface (Abstract, p. 2, paragraphs 0009 and 0012, p. 3, paragraph 0017). Shen et al. teach that the oligonucleotide tag can be identified without dissociation by hybridization analysis, wherein the tag is detected by contacting it with

an array of complementary nucleic acids immobilized on a support (p. 3, paragraphs 0021 and 0023). Therefore, it would have been obvious to one of skill in the art, at the time the invention was made, to determine the identity of the biomolecule from hybridization analysis of its attached oligonucleotide with the complementary oligonucleotide present on the bilayer expanse, as taught by Shen et al. with a reasonable expectation of success. One of skill in the art would have been expected to have a reasonable expectation of success in using such a method because the art teaches the successful use of oligonucleotide hybridization in determining the identity of oligonucleotide-tagged biomolecules.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

(10) Response to Argument

The rejection of claims 1-4, 6, 7, 9, 11, 12 and 22-25 under 35 U.S.C. 103(a) as being unpatentable over Boxer et al. (WO98/23948), in view of both Boukobza et al. (J Phys Chem, 2001, 105: 12165-12170) and Niemeyer et al. (DE 19902391).

It is noted that the appellant admits that the combination of references taken as a whole teaches a bilayer array as in Boxer et al. with a vesicle immobilized to the bilayer array through complementary nucleic acids as in Niemeyer et al. and Boukobza et al. (see the Appeal Brief, p. 6, first full paragraph). It is also noted that the appellant does not contest that one of skill in the art would have been successful in associating

receptors with vesicles such that their ligand binding site is located on the exterior of the vesicles.

The appellant argues that the combination of Boxer et al., Boukobza et al., and Niemeyer et al. cannot render the instant claims obvious because the combination fails to teach or suggest an array of separated lipid bilayer expanses including at least one vesicle associated with a receptor, wherein the vesicle is anchored to the lipid bilayer via a complementary oligonucleotide.

This is not found persuasive. As indicated in the rejection above, Boxer et al. teach a device comprising an array of separated lipid bilayer expanses with associated receptors having the ligand binding sites located on the exterior of the lipid bilayer. While Boxer et al. teach direct association of their receptors to the lipid bilayer expanses and not indirect association via vesicles, modifying their teachings by using the indirect association via vesicles is suggested by the prior art. Specifically, Boukobza et al. teach that directly immobilizing biomolecules on substrates modifies their dynamics via interaction with the substrate. Boukobza et al. teach overcoming the biomolecule-substrate interaction by associating the biomolecule with lipid vesicles and tethering the vesicles to a lipid bilayer expanse. Importantly, Boukobza et al. teach that the biomolecules can be membrane proteins (p. 12169, column 2, *Conclusion*). Thus, the teachings of Boukobza et al. provide not only the suggestion and the motivation, but also the means to avoid the interference by the substrate. Based on the teachings of Boukobza et al., one of skill in the art would have known that the direct immobilization of

receptors as in Boxer et al. would lead to interaction with the substrate and thus interference with the receptor-ligand interaction. One of skill in the art seeking to use the array of Boxer et al. for identifying ligands specific for their immobilized receptors would have been motivated to eliminate the receptor-substrate interaction and would have known to do so by replacing the direct association of receptors with the indirect association via lipid vesicles. The appellant did not provide any evidence to the contrary.

Furthermore, since tethering via oligonucleotide hybridization and its advantages were taught by the prior art (see the teachings of Niemeyer et al. above), one of skill in the art would have been motivated and would have found it obvious to tether the vesicles via oligonucleotide hybridization. Again, the appellant did not provide any evidence to the contrary.

Thus, the combination of Boxer et al., Boukobza et al., and Niemeyer et al. does teach an array of separated lipid bilayer expanses including at least one vesicle associated with a receptor, wherein the vesicle is anchored to the lipid bilayer via a complementary oligonucleotide.

The appellant argues that the examiner provided no reasoning for one of skill in the art to modify the combined teachings of Boxer et al., Boukobza et al., and Niemeyer et al. along an untaught and unsuggested path to arrive at the instant rejection is not found persuasive.

This is not found persuasive for the same reasons set forth above. Specifically, the rejection is not based on modifying Boxer et al., Boukobza et al., and Niemeyer et al. along an untaught and unsuggested path. The rejection is based on modifying Boxer et al. along a path that was taught and suggested by Boukobza et al. and Niemeyer et al.

The appellant argues that a challenge to using lipid bilayer arrays on a solid substrate for receptors is that the receptor can interact with the substrate, which interaction could cause denaturation and loss of function or could limit lateral mobility. By having the vesicle tethered to the bilayer expanse through complementary oligonucleotides as in the present claims, the vesicle and associated receptor are distanced from the substrate. The claimed array retains the benefit of spatial organization and lateral mobility, while retaining the function of the receptor.

In response, this was taught by the prior art (see the teachings of Boukobza et al. above, disclosing the advantage of distancing the biomolecules from the substrate by incorporating them into vesicles and tethering the vesicles to the substrate). Importantly, even the appellant admits that Boukobza et al. do each that the indirect anchoring method via vesicles tethered to the bilayer expanse overcomes the problem of molecule-surface interaction (see the Appeal Brief, p. 7). Based on the teachings of Boukobza et al., one of skill in the art would have known that distancing the receptors from the substrate would eliminate the interaction with the substrate and thus interference with the dynamics of the receptor-ligand interaction. Furthermore,

modifying Boxer et al. by including the advantageous indirect immobilization of Boukobza et al. would have necessarily resulted in an array exhibiting spatial organization and lateral mobility, while retaining the function of the receptor.

The appellant argues that, although Boxer et al. teach a lipid bilayer array with attached biomolecules, they do not mention that the biomolecules could be vesicles.

In response, it is noted that the instant rejection is an obviousness-type rejection and thus Boxer et al. do not have to teach each and every claim limitation. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The appellant argues that Boukobza et al. teach entrapped biomolecules and do not teach or suggest a vesicle including a receptor having the binding site located on the exterior of the vesicle. The appellant also argues that Boukobza et al. do not teach binding a test agent to the vesicle.

This argument is not found persuasive because it is directed to Boukobza et al. individually. Boukobza et al. do not have to teach each and every claim limitation. It is the combination of Boxer et al. and Boukobza et al. that teach a vesicle having a receptor with its binding site located on the exterior of the vesicle, wherein the receptor binds a test agent. Specifically, Boxer et al. teach associating transmembrane receptors to their bilayer expanses and using them to detect a selected ligand in a

mixture of ligands (specifically contacting the device with the ligand mixture and detecting the binding of the selected ligand to its receptor immobilized on the device). In order to interact with their ligands, the receptors associated with the lipid bilayer of Boxer et al. must necessarily have the ligand binding sites located on the exterior of the lipid bilayer. Furthermore, Boukobza et al. teach that directly immobilizing biomolecules on lipid bilayers substrates has the disadvantage of allowing the interaction between the biomolecules and the substrate. Boukobza et al. teach overcoming this interaction by indirect association, specifically associating the biomolecule with lipid vesicles and tethering the vesicles to a lipid bilayer substrate. Although the appellant argues that Boukobza et al. only teach entrapped biomolecules, this is incorrect as Boukobza et al. clearly teach their method as also being useful for associating membrane proteins (p. 12169, column 2, *Conclusion*). Based on these teachings, one of skill in the art would have known that the transmembrane receptors (which are membrane proteins) of Boxer et al. could be associated to the lipid bilayers by using the indirect association method taught by Boukobza et al. One of skill in the art would have found it obvious and would have been motivated to use the indirect association via vesicles in order to avoid the interaction between the transmembrane receptors and the lipid bilayer substrate. Furthermore, one of skill in the art seeking to use the lipid bilayer array for detecting specific ligands from a mixture as taught by Boxer et al., would have necessarily associated the receptors such that their binding sites are on the exterior of the vesicles to permit the specific interaction with and the identification of ligands. The appellant did not provide any evidence to the contrary.

Thus, the combination of Boxer et al. and Boukobza et al. does teach: **(i)** anchoring a vesicle having a receptor with its binding site located on the exterior of the vesicle and being capable of specifically binding a ligand (i.e., a test agent) above the lipid bilayer; and **(ii)** binding a test agent to the vesicles.

The appellant argues that one of skill in the art would not modify Boukobza et al. to include a receptor having the binding site located on the exterior of the vesicles.

This argument is not material to the instant rejection, which is based on modifying Boxer et al. by incorporating their transmembrane receptors into vesicles and not on modifying Boukobza et al.

The appellant argues that, since Niemeyer et al. do not teach a vesicle having a receptor with its binding site located on the exterior of the vesicle and being capable of specifically binding a ligand (i.e., a test agent) above the lipid bilayer, their teachings combined with Boxer et al. and Boukobza et al. do not show or suggest all features of claim 1.

This is not found persuasive. As set forth above, the combination of Boxer et al. and Boukobza et al. teaches anchoring a vesicle having a receptor with its binding site located on the exterior of the vesicle and being capable of specifically binding a ligand above the lipid bilayer. Furthermore, since Niemeyer et al. teach the advantages of anchoring via oligonucleotide hybridization as opposed to the avidin/biotin interaction, one of skill in the art would have been motivated to replace the avidin/biotin anchoring

of Boxer et al. and Boukobza et al. with anchoring via oligonucleotide hybridization. Thus, the combination of Boxer et al., Boukobza et al., and Niemeyer et al. does teach all limitations of claim 1.

The appellant argues that, although Niemeyer et al. teach immobilizing via oligonucleotide hybridization in order to use cost-intensive sensor surfaces several times, a lipid bilayer would not be reusable and the ability to immobilize many different macromolecules in one step does not suggest to one of skill in the art to modify the teachings by immobilizing via oligonucleotide hybridization.

This is not found persuasive because it is just an argument not supported by any evidence. Apart from an argument, the appellant did not provide any evidence that lipid arrays are not reusable. Specifically, the appellant did not provide any evidence that one of skill in the art would not have been successful in removing vesicles attached via reversible oligonucleotide hybridization with new vesicles comprising different receptors of interest, when needed. Furthermore, apart from an argument, the appellant did not provide any evidence indicating that one of skill in the art would not have been motivated to simplify the procedure of making the array by using oligonucleotide hybridization to immobilize many different macromolecules in one step.

Importantly, this argument is contradicted by the appellant's admission in the Appeal Brief:

> "At most, the combination of references taken as a whole can be said to teach a bilayer array as in Boxer et al. with a vesicle immobilized to the bilayer array through complementary nucleic acids as in Niemeyer et al. and Boukobza et al."

(Appeal Brief, p. 6, first full paragraph).

Thus, the examiner provided ample reasoning as to why, at the time the invention was made, one of skill in the art would have arrived at the claimed invention by modifying Boxer et al. according to the teachings and suggestions of Boukobza et al. and Niemeyer et al.

The rejection of claims 1-4, 6, 7, 9-12 and 22-25 under 35 U.S.C. 103(a) as being unpatentable over Boxer et al. taken with both Boukobza et al. and Niemeyer et al., in further view of each Cornell et al. (U.S. Patent No. 5, 874,316), Arnold et al. (U.S. Patent 5, 310, 648), and Bayerl et al. (U.S. Patent No. 6,051,372).

The appellant argues that the teachings of Cornell et al., Arnold et al., and Bayerl et al. do not provide the missing teachings of Boxer et al., Boukobza et al., and Niemeyer et al.

This is not found persuasive because, as set forth above, there is no missing teaching in the combination of Boxer et al., Boukobza et al., and Niemeyer et al.

The rejection of claims 1-4, 6-9, 11, 12 and 22-25 under 35 U.S.C. 103(a) as being unpatentable over Boxer et al. taken with both Boukobza et al. and Niemeyer et al., in further view of Shen et al. (PGPUB 2003/0148335).

The appellant argues that the teachings of Shen et al. do not provide the missing teachings of Boxer et al., Boukobza et al., and Niemeyer et al.

This is not found persuasive because, as set forth above, there is no missing teaching in the combination of Boxer et al., Boukobza et al., and Niemeyer et al.

In conclusion, the instant claims and disclosure encompass and rely on compositions known in the art to practice the claimed invention. At the time of filing, arrays of separated lipid bilayers including transmembrane receptors associated with the lipid bilayers, wherein the receptors have the ligand binding site outside the lipid bilayer and capable of specifically binding a test agent were taught and used by Boxer et al. The only difference between the array of Boxer et al. and the claimed invention is that Boxer et al. do not teach attaching their transmembrane receptors via associating them to vesicles and tethering the vesicles to the lipid bilayer via oligonucleotide hybridization. However, using and the advantage of using vesicles to attach membrane proteins to lipid bilayers was taught by the prior art. Similarly, using and the advantage of using oligonucleotide hybridization to attach vesicles to substrates was taught by the prior art. One of skill in the art would have known and would have found it obvious to modify the array of Boxer et al. by incorporating these advantageous teachings in the prior art. The appellant did not provide any evidence to the contrary. Please note that that the appellant does not contest that receptors can be successfully associated with lipid vesicles or that lipid vesicles can be successfully associated to lipid bilayers via oligonucleotide hybridization.

In fact, the appellant himself admits that the combination of the cited art teaches a lipid bilayer array with vesicles immobilized to the bilayer array through

complementary nucleic acids (see the Appeal Brief, p. 6, first full paragraph). The only issue that the appellant argues, specifically that the combination of references does not teach that the vesicles are associated with a receptor having its binding site located on the ***exterior*** of the vesicle and being capable of specifically binding a test agent above the lipid bilayer, is incorrect. As set forth above, by modifying the array of Boxer et al. via advantageously associating their transmembrane receptors with vesicles, one of skill in the art would have obtained an array with vesicles associated with receptors having their binding site located on the exterior of the vesicle and being capable of specifically binding a test agent, as instantly claimed.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Ileana Popa/
Primary Examiner, Art Unit 1633

Conferees:
/Joseph T. Woitach/
Supervisory Patent Examiner, Art Unit 1633

/Gary Benzion/
Supervisory Patent Examiner, Art Unit 1637